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Bilateral Cochlear Implants in Children

- Clinical and Methodological Studies

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Stockholm 2015

To my wife, and my many and fabulous children

“I’m a lucky man, to count on both hands, the ones I love”

Eddie Vedder

ABSTRACT

A cochlear implant (CI) restores functional hearing in individuals with bilateral severe-to-profound sensorineural hearing loss. Despite hearing loss in both ears, CIs are usually provided unilaterally, excluding the alleged benefits associated with bilateral auditory stimulation. Recently, however, bilateral cochlear implantation is increasingly common, with the main objectives of enhancing sound localization abilities and speech recognition, particularly in the presence of background noise. Here, using a within-subject longitudinal design in a large clinical study sample of children using bilateral cochlear implants (BiCI), a large, sustained, and significant bilateral benefit in horizontal sound localization accuracy (SLA) was demonstrated. A significant bilateral benefit also existed in speech recognition in noise spatially separated from the target signal. Speech recognition in quiet, however, was comparable under BiCI and unilateral CI listening conditions. Parental reports corroborated behavioral findings. Yet, the bilateral benefit was not uniform across subjects, large intersubject variability existed both with BiCI and unilateral CI, and neither SLA, nor speech recognition performance, was restored to that found in children with normal hearing (NH). Clinically important, a significant improvement of horizontal SLA with increasing BiCI experience (21 percentage points per year) was demonstrated from onset of bilateral stimulation until about 3 years post bilateral implantation ($r = -0.51$, $p < 0.0001$, $n = 66$), with a very similar developmental rate observed intraindividually (mean of the individual slopes = 19 percentage points per year of BiCI experience, $n = 21$), suggesting an experience-driven maturation of SLA. Of further clinical importance, no relationship between SLA and age or age at implantations was found, albeit, improvements in SLA as a function of BiCI experience were faster, and the bilateral SLA benefit was larger, when bilateral implantation occurred before 4 years of age.

In an attempt to accommodate measurements of spatial hearing to clinical requirements, a SLA method using objectively recorded gaze was developed. Pupil positions toward spatially distributed auditory and visual events were recorded using corneal reflection eye tracking technique. The spatial resolution of the methodology allowed detailed objective analyses of gaze patterns in NH listeners from 6 months of age. SLA was rapidly measured in children (age range = 29 – 157 weeks; mean = 168 seconds, $n = 12$) and adults (mean = 162 seconds, $n = 8$). Data showed immature SLA in children, with increasing performance as a function of age ($r = -0.68$, $p = 0.015$). Highly reliable results existed in adults, who revealed high SLA across the entire spatial range tested.

The findings in this thesis have important methodological implications for the clinical management of children with CI, and provide valuable data which may be used in counseling prior to bilateral cochlear implantation. Moreover, the objective and rapid SLA methodology may aid clinicians at an early stage of the process of early intervention with cochlear implants and/or hearing aids in children with hearing loss.

LIST OF PUBLICATIONS

I. Horizontal Sound Localization in Children With Bilateral Cochlear Implants: Effects of Auditory Experience and Age at Implantation. Otology & Neurotology, 2011, 32, 558-564

II. Bilateral versus unilateral cochlear implants in children: Speech recognition, sound localization, and parental reports. International Journal of Audiology, 2012, 51, 817-832

III. A longitudinal study of the bilateral benefit in children with bilateral cochlear implants. International Journal of Audiology, 2015, 54, 77-88

IV. Corneal-Reflection Eye-Tracking Technique for the Assessment of Horizontal Sound Localization Accuracy from 6 months of Age. Ear and Hearing, 2015, Published ahead of print

ABBREVIATIONS

BiCI	Bilateral cochlear implants
SLA	Sound localization accuracy
BestCI	The single CI (left or right) which gives the highest speech recognition in quiet
SNR	Signal-to-noise ratio
dB	Decibels
SPL	Sound Pressure Level
Raus	Rationalized arcsine units
PTT	Pure-tone threshold
CI-1	The first implanted cochlear implant
CI-2	The second implanted cochlear implant
CI	Cochlear implant
NH	Normal hearing
SRM	Spatial release from masking
MSO	Medial superior olive
EI	Error Index
OC	Olivocochlear

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1. INTRODUCTION

The cochlear implant (CI) is the only auditory prostheses that can restore functional hearing in individuals with severe-to-profound bilateral hearing loss. More than 100 000 children use CIs worldwide [1], with remarkable outcomes including open set speech recognition [e.g. 2, 3] and successful language development [e.g. 4, 5]. The majority of children with CI, however, are implanted in one ear [6], despite experiencing bilateral auditory deprivation. This approach excludes the possible benefits afforded by hearing from two ears – binaural hearing. Binaural hearing is of major importance for spatial hearing capacities in individuals with normal hearing (NH). It facilitates segregation of a target voice from spatially separate competing voices, enables accurate horizontal sound localization, and promotes recognition of speech in a background of competing noise [7-10].

This thesis revealed distinct bilateral sound localization and speech recognition in noise benefits in children provided with bilateral cochlear implants. Studied longitudinally, the bilateral benefit appeared sustained, albeit, absolute bilateral and unilateral performance was worse than that of children with normal hearing and interindividual variability was high. From the onset of bilateral implantation, sound localization accuracy (SLA) seemed to undergo an experience-driven development, demonstrated in a large clinical study sample both on group level and intraindividually. Similarly, infants with normal hearing showed immature SLA with systematic improvements related to increasing age, as found in the course of the development of a rapid, objective and reliable method for the assessment of SLA suitable from 6 months of age.

1.1 Spatial Hearing

Unlike the visual system, where a topographic map of space is represented on the retina, no representation of auditory space exists in the sensory organ of hearing – the cochlea. Nonetheless, humans localize sounds along the horizontal dimension with precision [10-12] and understanding of speech in competing noise is greatly facilitated by spatial separation between the target signal and competing sound-sources compared with conditions where the signal and the noise are co-located [e.g. 7, 13]. This spatial release from masking (SRM) may result in >10 dB increase in speech reception threshold in listeners with NH [e.g. 9, 14]. Children demonstrate SRM and SLA similar to adults by age 5 to 6 years [15, 16].

To a large part, spatial hearing skills rely on cues arising as a result of how the incoming sounds interact with the head, torso and the two ears. These cues are processed in the central auditory system, and two of them – interaural level differences (ILDs) and interaural time differences (ITDs) – are binaural. Both cues are detected and encoded in the superior olivary complex in the auditory brainstem (ITDs in the medial superior olive (MSO) and ILDs in the lateral superior olive) [17, 18]. ILDs arise because the acoustic shadow caused by the head reduces the intensity of the sound at the side of the head farthest away from the sound-source. Intuitively, ILDs are frequency-dependent. Sound frequencies > 3000 Hz will result in large ILDs because of their relatively short wavelengths, while low-frequency sounds produce small ILDs as the relatively long wavelengths "bend" around the head, thus reaching the far ear [10, 19, 20]. By contrast, ITDs – generated as the distance between the two ears will delay the sound in the ear farthest from the source (also resulting in ongoing interaural phase differences) – are especially useful below about 1500 Hz [21]. For low-frequency tones, as an ideal example, the inputs to the MSO are phase-locked to the stimulus wave-form [22] resulting in synchronous nerve firing patterns. This synchrony – alongside a model proposed by Jeffress [19] which postulates a systematic arrangement of axons of variable length from each ear ("delay lines"), so that different coincidence-detector neurons encode different ITDs – has long been thought to lay the foundation for the intriguingly high sensitivity to ITDs in humans (in the order of some microseconds) [23]. However, the model by Jeffress, which has been established for more than 50 years, has recently been questioned by experimental data from mammals, suggesting that ITD tuning in the MSO of the Mongolian gerbil is the result of interaction of precisely timed excitatory and inhibitory inputs [24], and no direct confirmation of a "delay line" arrangement exists for the mammalian MSO.

Spectral cues (which may be monaural) are also utilized by the auditory system for spatial hearing, for example sound localization in the vertical dimension [25]. The shape of the pinna acts like a passive filter so that certain frequencies in the sound will be attenuated or amplified depending on the location of the sound-source, which also helps in resolving if a sound is coming from the front (0 degrees azimuth) or from the back (180 degrees azimuth) where ITD and ILD are zero.

Further advantages of having two ears include the effects of “binaural summation” and “better ear”. Because of stimulation of both ears, the auditory system can process two signals which introduce redundancy in information processing (binaural summation). The effect of “better ear” occurs when a target sound (e.g. speech) and noise are separated spatially so that the listener may attend to the ear with the more favorable signal-to-noise ratio (SNR).

1.2 Cochlear Implants

Unlike NH, where sound travels from the outer ear through the middle ear to the cochlea, where it is converted to electrical impulses, a CI directly stimulates the auditory nerve with electrical biphasic pulses. The CI system consists of an externally worn audio processor and an implanted receiver/stimulator attached to an electrode array which is surgically inserted into the scala tympany of the cochlea (Figure 1).

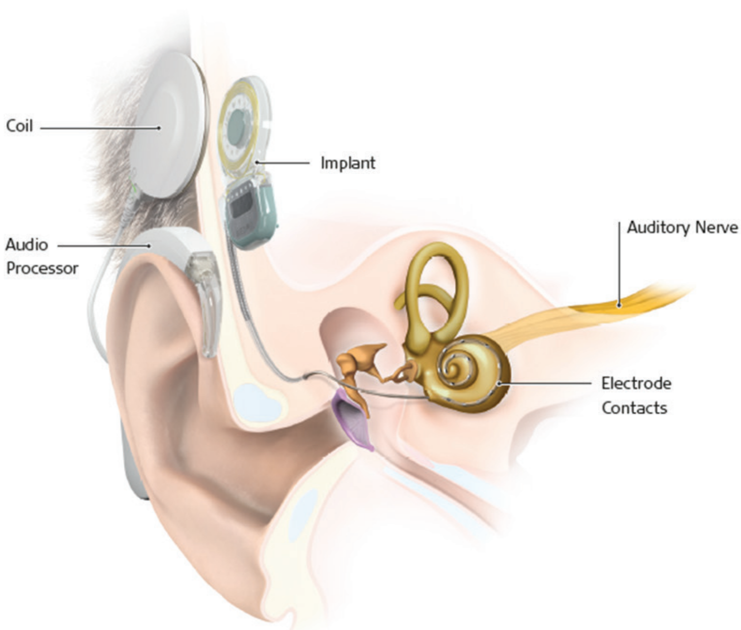


Figure 1. Schematic illustration of a cochlear implant system *in situ*. The external equipment (audio processor and coil) extracts the surrounding sound and converts it to a digital code which is transcutaneously transmitted to the implant via an inductive link. The implant decodes the signal and sends biphasic, interleaved electrical pulses to the electrode contacts inserted in the cochlea, resulting in direct electrical stimulation of the auditory nerve cells. Figure printed with permission from MED-EL © 2015.

The audio processor, which basic components are a microphone, a processing unit and a transmitting coil (Figure 1), is responsible for extracting features of the surrounding sound and converting them to a digital code. The digital code is transcutaneously transmitted by the coil – which is attached to the implant by a magnet – via radio frequency to the implanted receiver. The digital code contains the parameters used by the implant for appropriate electrical stimulation. The electrical currents, sent to the contacts on the electrode array, stimulate the auditory nerve that projects from the cochlea to the central nervous system. The electrical stimulation of the auditory nerve is interpreted as sound.

The modern multi-channel CI system exploits the tonotopic organization of the cochlea – the basal end of the cochlea encodes high frequencies and the apical part of the cochlea encodes low frequencies. Briefly, a set of band pass filters divides sound into different frequency bands, each of which correspond to a place of stimulation in the cochlea. The envelope of the signal in each band is extracted and then compressed (often logarithmically) to match the limited electrical dynamic range in current CI systems [about 10 dB, see 26]. The compressed envelopes modulate the interleaved current pulses that stimulate the auditory nerve fibers. While this "place-pitch" approach often results in high level of speech understanding in quiet conditions and allows children with severe-to-profound congenital bilateral sensorineural hearing loss to develop hearing, speech and language [e.g. 27, 28], it lacks several of the fundamental aspects found in the process of normal hearing. As an example, the healthy cochlea performs a detailed frequency analysis of the incoming sound by virtue of the basilar membrane micromechanics and outer hair cell motility [29, 30]. As a result, synapses of each inner hair cell deliver highly filtered signals to between 10 and 30 auditory neurons [31]. With electrical stimulation in the cochlea, such fine frequency resolution is not possible due to spread of current [32]. Hence, spectral resolution in implant listeners is inadequate and thought to be a major limiting factor for performance [e.g. 33, 34]. As another example, the compression of the incoming signal to match the acoustical dynamic range (100 – 120 dB) to the electrical dynamic range (about 10 dB) seem to reduce speech recognition in noise [35].

1.3 Bilateral Cochlear Implants

The clinical rationale for bilateral cochlear implantation is several-fold, with safety being one important reason. An individual with BiCI have a reduced risk (compared to being unilaterally implanted) of a “silent period” if technical malfunction should occur, since it is unlikely that both implants and/or audio processors fail simultaneously. Furthermore, given the lack of prognostic factors for implantation, it is not always straightforward which of the two ears to implant. For example, recent models only account for about 20% of the variability in speech recognition performance [36, 37]. The main goal of bilateral implantation, however, is to restore some of the abilities that rely on binaural hearing in NH listeners. Specifically, bilateral implantation seeks to improve sound localization abilities and speech recognition in acoustically challenging environments.

Accumulating data support BiCI in children, as shown by comparing BiCI and unilateral cochlear implant (UCI) performance intraindividually [28, 38-41], or between groups of children using BiCIs and UCI [15, 42, 43]. These studies, and recent meta-analysis of current knowledge [44, 45], indicate that speech recognition in noise and SLA is promoted by BiCI. However, neither adults nor children using implants perform as well as NH listeners [e.g. 41, 46, 47] and the magnitude of the bilateral benefit (BiCI minus UCI performance) shows large intersubject variability. The bilateral speech recognition in noise benefit, for example, ranges from a few percent to about 40% [28, 44, 45]. Furthermore, documented cases exists that show deterioration in performance using BiCI [see e.g. Figures 3 and 4 in 28].

1.3.1 Limitations in Bilateral Cochlear Implant Stimulation and Intervention

Performance with BiCI is limited for several reasons. Temporal fine-structure is not well preserved in current CI systems, resulting in lack of ITD cues presented to the user [see 48 for an overview]. ITD cues may still be present in the envelopes of the signals, but the left and right CI systems are independent in their sampling of the sound, and stimulation of the auditory neurons, which alter ITD cues. ILD cues may also be distorted due to the separate nature of the two systems (e.g. automatic gain control settings and microphone responses may differ interaurally). Moreover, the current surgical approach for cochlear implantation is not accurate enough to achieve interaural matching of insertion depth and electrode placement, affecting lateralization of sound as shown in both NH listeners and individuals with CI [49].

While technical and surgical limitations may account for the gap in performance between listeners with CI and NH – and to some extent for the large intersubject variability in, for example, sound localization abilities – delayed and/or atypical auditory experience during sensitive or critical periods in development is also a likely limiting factor for performance and contributes to the variability across subjects. Animal data suggest that ITDs and ILDs are disrupted by an abnormal acoustic environment during development [50, 51]. However, a remarkable degree of plasticity in the auditory system may still allow a development in performance, as demonstrated by monaural earplugging experiments in juvenile ferrets [52], in NH children at the level of the brainstem [53], and at the level of the cortex in children with CI [54, 55]. The development of sound localization abilities specifically, seem to be dependent on relevant auditory experience and training for shaping the necessary neural circuits and developing accuracy [e.g. 55, 57].

2. AIMS

The overall aims of this thesis were to characterize the development of sound localization accuracy and speech recognition in multi-source noise in children with bilateral cochlear implants, to quantify the bilateral benefit after bilateral cochlear implantation, and to utilize an immature auditory system – as in infants, and in children with severe-to-profound hearing loss – as an approach for the study of the development of sound localization.

Paper I. The aim was to study the effects of auditory experience and age at implantation(s) on horizontal SLA in a large, consecutive sample of children using bilateral cochlear implants. The heterogeneity in ages at implantations and chronological age in the study sample at the time of assessment allowed analyses of the alleged effects of age at implantation, time elapsed between implantations, and the BiCI experience.

Paper II. The main purpose of this study was to determine the bilateral speech recognition and sound localization benefit in children with BiCIs. To this end, speech recognition in quiet and in spatially separate competing noise as well as SLA was measured in sound field under binaural and monaural listening conditions. Paper II presents cross-sectional results of a longitudinal study.

Paper III. This longitudinal study was motivated by the fact that the long-term individual bilateral benefit remains relatively unexplored. The aim was to identify if the bilateral speech recognition and sound localization benefit was developing with increasing auditory experience after several years of BiCI use.

Paper IV. The aim of this study was to develop a fast, valid, and objective method for the assessment of SLA from six months of age.

3. SUBJECTS AND METHODS

3.1 Subjects

In all studies in this thesis, written informed consent was obtained from parents of the participating children and adult participants. In children who were determined to have the ability to give informed assent, this was obtained.

3.1.1 Paper I

The formal inclusion criterion for the study was to be a user of BiCI. A total of 88 children were implanted bilaterally with CIs at Karolinska University Hospital from March 2002 to May 2007. Twenty-two of these children were excluded because they were too young to understand the instructions associated with the test, did not comply with the test protocol, moved to other clinics, or stopped using one CI. The final sample included 66 children with BiCI who participated at a median age of 5.6 years (range = 2.8 – 17.3 years).

3.1.2 Papers II and III

In this two-center longitudinal project, which was a collaboration between the cochlear implant centers at Karolinska University Hospital and Linköping University Hospital, formal inclusion criteria declared that children were required to be: aged 5 – 12 years at the start of the study, daily users of BiCI, and understand the instructions associated with the tests. Eighty-five children fulfilled the age criterion (Linköping, n = 19; Karolinska, n = 66). Seven children were excluded because participation was deemed impossible based on an audiologist's earlier experience testing the child, or BiCI use was reported to be minimal, or because of a failure to produce a complete test (BiCI versus unilateral CI) in any of the tests at any of the three annual assessments. The remaining 78 subjects participated at least in one test at one visit at a mean age of 7.8 years (range = 5.1 – 11.9 years), 8.8 years (6.0 – 13.1), and 9.8 years (7.0 – 14.0) at the three annual visits, respectively. Longitudinal relative data (BiCI versus unilateral CI) were available for a subset of the children for speech in quiet (n = 48), speech in noise (n = 37), and SLA (n = 34) and further analyzed separately.

Children with normal hearing aged 4.8 – 9.0 years (mean age = 6.8 years, n = 30) was recruited to provide normative cross-sectional data for the tests used in the study. Normal hearing was defined as hearing thresholds of 20 dB HL or better at octave frequencies from 0.5 to 4 kHz in both ears according to

ISO 8253-1:2010. They were not matched for age or gender with the group of children using BiCI.

3.1.3 Paper IV

Eight healthy adult volunteers aged 18 – 40 years who had pure-tone thresholds (PTTs) ≤20 dB HL in both ears at 125, 250, 500, 1000, 2000, 3000, 4000, 6000, and 8000 Hz, and 12 infants and young children aged 29 – 157 weeks who passed the universal newborn hearing screening participated in this study. Adults were otologically normal as confirmed by otomicroscopy, tympanometry and acoustic stapedius reflex measurements. Children had no history of frequent ear infections, according to parental reports.

3.2 Methods

3.2.1 Design

In paper I, SLA was measured in a consecutive sample of children with BiCI (n = 66), and repeatedly (3 to 6 occasions) in a subset of these children (n = 21), allowing retrospective analyses of cross-sectional and longitudinal data.

In papers II and III, SLA and speech recognition data from children with BiCI were collected prospectively in a 2-year longitudinal design including 3 assessments. Parental reports were collected at the start of the study. Data from children with normal hearing were collected once.

In paper IV, SLA data were objectively and prospectively collected at one occasion. Adult data were collected to provide a comparison with infants. Test reliability was quantified by analyzing the variability in test – retest differences.

3.2.2 Sound Localization Accuracy

3.2.2.1 Test environment

SLA measurements in children with BiCI and in normal hearing children were performed either in an anechoic chamber (Linköping) or in a sound treated room (4.1 x 3.5 x 2.5 m, Karolinska) with an ambient sound level of 30 dB(A) and short reverberation time (T30 = 0.12 s at 0.5 kHz). SLA in infants, toddlers, and adults was assessed in an audiological test room (4.1m x 3.3m x 2.1m) with low ambient sound level (25 dB (A)), and short reverberation time (T30 = 0.11 seconds at 0.5 kHz).

3.2.2.2 Sound Localization Accuracy Measurements in Children with Bilateral Cochlear Implants and in Children with Normal Hearing (Papers I, II, III)

Children were seated comfortably in a chair facing 5 loudspeakers spanning a semi-circle from -90 degrees to 90 degrees azimuth in increments of 45 degrees (Figure 2, panel b). A SLA measurement consisted of 10 presentations of the auditory stimulus from any one of the loudspeakers in random order (2 presentations per loudspeaker). The stimulus was presented at 65 dB SPL and randomly roved within ±5 dB to limit access to monaural level cues. Children were required to indicate the perceived sounding loudspeaker verbally or by pointing. All children received a short task-specific training, which consisted of one presentation of the stimulus per loudspeaker with feedback.

In paper I, subjects listened to pink noise pulse trains using BiCI. The pulse trains had slightly varying frequency content from trial to trial to limit the possibility of using monaural spectral cues for localization.

In paper II and paper III, subjects listened to two recorded and filtered animals sounds (dog barks with energy mainly below 1 kHz, and cricket chirps with energy mainly between 2.5 – 5.0 kHz). Children with BiCI were tested using BiCI and the single CI which gave the highest speech recognition in quiet (BestCI). Thus, SLA was assessed four times (2 x 2). The order of tests was randomized and balanced. Children with NH were tested with the same stimuli with both ears open (BiNH) and unilaterally (UniNH) by plugging the left (n = 15) or the right (n = 15) ear with an ear-plug with the addition of an ear muff.

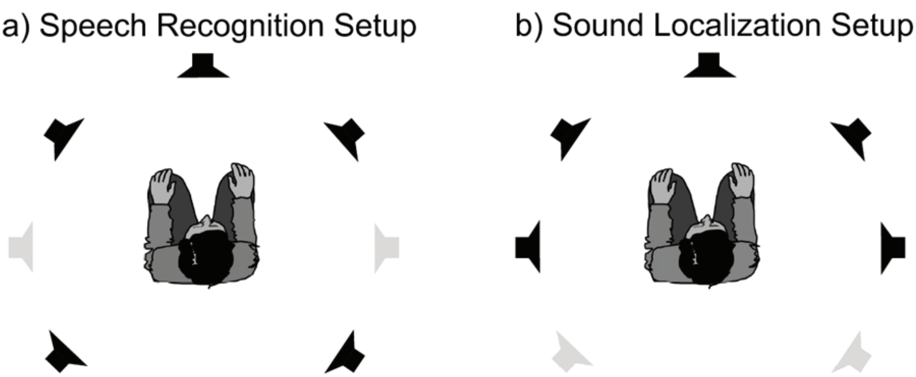


Figure 2. Loudspeaker setups for the speech recognition (a) and sound localization (b) tests. Grey loudspeakers were not in use. Speech recognition in quiet was measured with the loudspeaker in front of the child. Speech-weighted stationary noise was presented from loudspeakers at ±45 degrees azimuth and ±135 degrees azimuth during the speech recognition in noise test. The loudspeakers in the sound localization test setup were separated by 45 degrees spanning a semi-circle from -90 degrees to 90 degrees azimuth. From Asp et al. (2012), *Bilateral versus unilateral cochlear implants in children: speech recognition, sound localization, and parental reports, International Journal of Audiology*, 51:11, 817-832, published by Taylor & Francis.

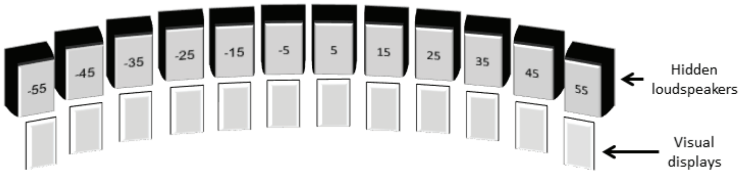
3.2.2.3 Monte Carlo Simulation for the Determination of the Variance for Random SLA performance

A Monte Carlo simulation was conducted to determine the 95% confidence interval for random sound localization performance for the setup and presentation paradigm (i.e. 5 loudspeakers, 2 presentations per loudspeaker in random order) used in children with BiCI and normal hearing. The simulation was based on one million simulated stimulus presentations and random responses and revealed a mean (SD) EI = 1.0 (0.23) (95% two-sided C.I. = [0.54, 1.46]). Thus, an EI < 0.54 was considered to demonstrate SLA significantly higher than random performance ($p < 0.05$).

3.2.2.4 Sound Localization Accuracy Measurements in Infants and Adults

Horizontal SLA in infants and adults with NH was objectively quantified in sound field by recording the gaze of the tested subject towards 12 spatially separate visual displays, mounted below 12 active loudspeakers, resulting in 12 loudspeaker/display-pairs (LD-pairs) (Figure 3a).

a)



b)

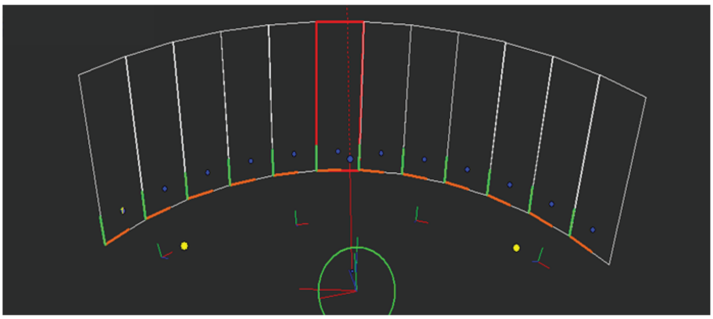


Figure 3. a) The sound localization setup consisted of 12 loudspeaker/display-pairs, arranged in 10 degrees increments, spanning ±55 degrees in the frontal horizontal plane. b) The three-dimensional model of the 12 "Areas of Interest" (AOI; virtual rectangles incorporating the loudspeakers and the visual displays). The gaze of a participating subject is here displayed as a red gaze vector toward the AOI corresponding to -5 degrees azimuth. From Asp et al. (2015), *Corneal-Reflection Eye-Tracking Technique for the Assessment of Horizontal Sound Localization Accuracy From 6 Months of Age,* Ear & Hearing (published ahead of print by Wolters Kluwer Health Lippincott Williams & Wilkins).

The LD-pairs were placed in an audiological test room at 10 degrees intervals in the frontal horizontal plane (±55 degrees azimuth). An ongoing auditory-visual stimulus was presented at 63 dB SPL(A) and shifted to randomized LD-pairs simultaneously with pauses of the visual stimulus (totally 24 sound-source shifts). The visual stimulus was automatically reintroduced at the azimuth of the sounding loudspeaker after a sound-only period of 1.6 seconds (Figure 4), a time-window which was based on pilot-testing and findings from head-turn experiments in 6-18 months old infants [58].

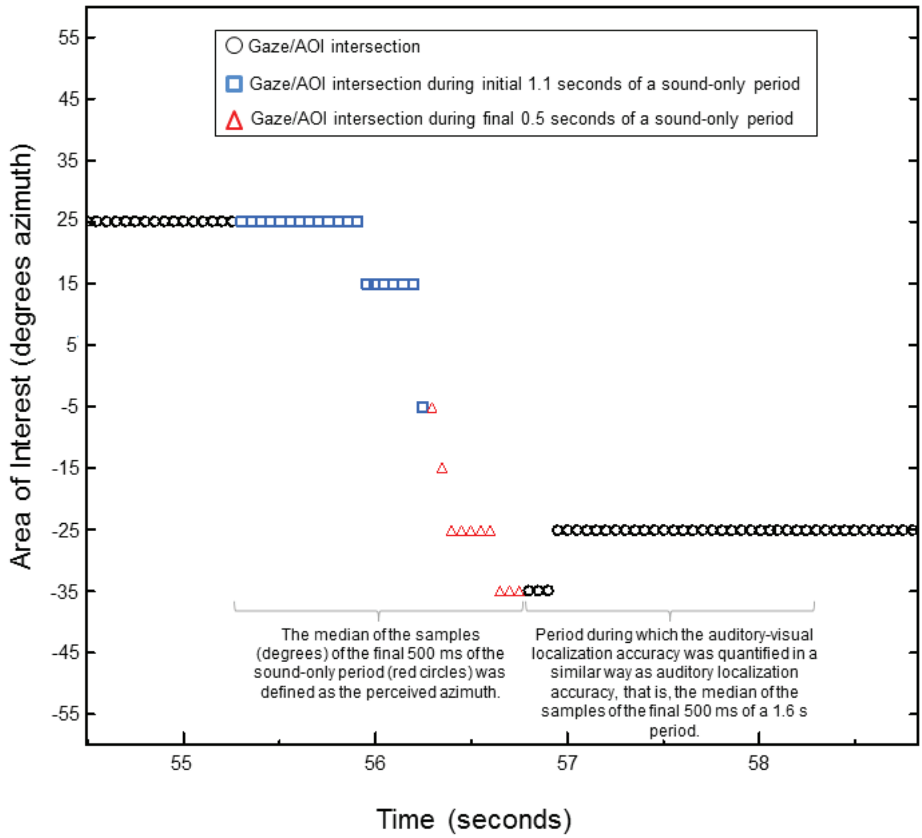


Figure 4. Gaze/AOI intersection samples from a 4.3 second time window of a sound localization test in a 24 months old child, demonstrating sustained acquisition of gaze toward the AOIs. In this example, a randomized shift of the auditory-visual stimulus from the loudspeaker and visual display at 25 degrees azimuth to -25 degrees azimuth was initiated. The gaze of the child (markers) was sampled at 20 Hz. Black circles illustrates gaze samples during the auditory-visual stimulus, while blue squares and red triangles illustrates gaze samples during a sound-only period of 1.6 seconds. During the sound-only period, the subject was guided by audition only to pinpoint the origin of the sound. The median azimuth of the final 500 ms (red circles) of the sound-only period was defined as the perceived azimuth. During a 1.6 second period after the transient reappearance of the visual part of the stimulus, gaze samples were stored in order to calculate auditory-visual localization accuracy, which was computed in the same way as the sound localization accuracy.

A corneal reflection (CR) eye tracking technique allowed acquisition of the subjects' pupil positions relative to the LD-pairs at a sampling rate of 20 Hz. The perceived azimuth was defined as the median of the intersections between gaze and Areas of Interest (AOI) – a 3D definition of the LD-pairs in the eye-tracking software (Figure 3b) – during the final 500 milliseconds of the sound-only period (see red triangles in Figure 4).

In order to control for oculomotor immaturity in the tested age range, the perceived auditory-visual azimuth was computed in a similar way as the perceived auditory azimuth, i.e. as the median of the final 10 samples (500 milliseconds) of a 1.6 second period after the transient reappearance of the visual stimulus (Figure 4).

To determine test reliability a retest was performed in adults, while test reliability in children was estimated by splitting each SLA test in part 1 (“test”) and part 2 (“retest”). The statistical reliability of the SLA test was then quantified by analysis of the variability in test-retest differences, and by estimation of the variance in EI for a single SLA measurement in both children and adults (see Paper IV for a detailed description of the variance estimations). Briefly, the equations for the variance estimates were

$$S^2\,[EI] = \frac{Y^2}{4NK} \qquad (1)$$

in children, and

$$S^2\,[EI] = \frac{var[test\text{-}retest]}{2} \qquad (2)$$

in adults, where Y = the square sum across all infants “test” –“retest” differences, weighted with the number of perceived sound-sources per subject, N = the number of subjects, K = the number of sound presentations in a full test, and var is the variance based on the collected test-retest samples.

3.2.2.5 Quantification of Sound Localization Accuracy (Papers I, II, III, IV)

SLA was quantified by an Error Index (EI) [see e.g. 54, 55, 56]. The EI ranges from 0 (perfect performance) to 1 (random performance) and takes into account how far away from the actual sound-source a subject is indicating the perceived sound direction according to:

$$EI = \frac{\sum_{(i,k)\in P} |i-k|}{\left(\sum_{i\in P}\sum_{k=1}^{n} |i-k|\right)/\mathrm{n}} \qquad (3)$$

where P is the set of loudspeakers that are available in the setup, i = the presented loudspeaker (1, 2, …), k = the perceived loudspeaker (1, 2, …), and n = the number of loudspeakers. The EI has an advantage in setups with large angular separations (where it may be less relevant to report mean angular errors) and facilitates comparison across setups.

3.2.3 Speech Recognition in Children with Bilateral Cochlear Implants and in Children with Normal Hearing (Papers II, III)

3.2.3.1 Test environment

Speech recognition was measured either in an anechoic chamber (Linköping) or in a sound treated room (4.1 x 3.5 x 2.5 m, Karolinska) with low ambient sound level (30 dB(A)) and short reverberation time (T30 = 0.12 s at 0.5 kHz).

3.2.3.2 Speech material

The speech material comprised 8 monosyllabic word-lists including 25 words each. The word-lists, derived from a standardized Swedish clinical speech audiometry test [62], were phonemically balanced and recorded with a female voice with a typical spectrum, i.e. no reduction of spectral energy at high frequencies [63]. Subjects were familiarized with the speech material by allowing training on a word-list that was not used in subsequent testing.

3.2.3.3 Speech Recognition in Quiet

The speech signal was presented at 65 dB SPL from a loudspeaker in front of the subject (Figure 2, panel a). Children were instructed to repeat what they heard and guessing was encouraged. In children with BiCI, speech recognition was measured with left and right CI and with BiCI (3 tests). The single CI which gave the highest speech recognition score was denoted BestCI. The order of tests was randomized and balanced. In children with normal hearing, speech recognition was measured with BiNH and UniNH (left ear, n = 15; right ear, n = 15) and the order of tests was randomized and balanced.

3.2.3.4 Speech Recognition in Multi-Source Noise

The speech signal was presented at 65 dB SPL at 0 degrees azimuth simultaneously with 4 uncorrelated, stationary, speech-weighted (same long term spectrum as the speech) noise signals at ±45 and ±135 degrees azimuth. The rationale for the spatial separation of the noise sources from the target signal was so that SRM could occur. The fixed signal-to-noise ratio (SNR) was 0 dB. Children were instructed to repeat back what they heard and guessing was encouraged. In children with BiCI, speech recognition in noise was measured with BiCI and with BestCI (2 tests) and the order of tests was randomized and balanced. In children with normal hearing, speech recognition was measured with BiNH and UniNH (left ear, n = 15; right ear, n = 15) and the order of tests was randomized and balanced.

3.2.3.5 Transformation of Speech Recognition Scores (Papers II and III)

In order to make the speech recognition scores (percent correct) suitable for statistical analysis on both group and individual level they were transformed to rationalized arcsine units (raus), according to the transform proposed by Studebaker [64]. The main benefits of the transformation are: 1) it reduces the correlation between mean values and the sample variance contributing to the means, and 2) the standard error of the difference between two speech recognition scores does not vary with the values of those scores. Thus, the difference between for example 82 and 92 raus is as significant as the difference between 62 and 52 raus. This is not the case with proportionate scores. Raus are numerically similar to percent and a critical difference at 95% confidence level between two speech recognition scores was 25.3 raus in Papers II and III.

3.2.4 Parental Reports (Papers II, III)

A questionnaire was administered to the parents of the children with BiCI to collect data regarding the decision before a second implant (in case of sequential cochlear implantation), benefit from the second implant, and device use. In addition, parents were asked in the questionnaire to rank the speech recognition and sound localization abilities of their children in daily situations using a single CI and BiCI. The ranking was from 1 to 4. Questions were formatted so that a higher rank related to better hearing performance (see Appendix online in Paper II).

3.2.5 Hearing Thresholds (Papers II, III, IV)

In children with BiCI, left and right sound-field hearing thresholds were measured by presenting frequency-modulated tones at 250, 500, 1000, 2000, 4000, and 6000 Hz, as an integrity test of the CI system. In children with normal hearing, left and right PTTs at 500, 1000, 2000, and 4000 Hz were measured using headphones (TDH 39). Adult PTTs were measured at 125, 250, 500, 1000, 2000, 4000, 6000, and 8000 Hz using headphones (HDA 200) and a computerized fixed-frequency Békésy technique [65].

3.2.6 Statistical Analyses

Linear and multiple regression analyses were used to study any effects of age (years), age at implantations (years), BiCI experience (years), and interimplant interval (years) on SLA and speech recognition in quiet and in noise in children with BiCI.

Within-subject analyses of speech recognition performance (raus) and SLA (EI) were performed in children with cochlear implants (BiCI versus BestCI) and in children with normal hearing (BiNH versus UniNH) using Student's t-test for dependent samples. Between-subject analyses (CI versus NH) were performed using Student's t-test for independent samples.

Within- and between-subject comparison of medians was performed using Wilcoxon matched pairs tests and Mann-Whitney U tests, respectively.

4. RESULTS

4.1 Bilateral Versus Unilateral Spatial Hearing in Children With BiCI (Papers II, III)

4.1.1 Sound Localization Accuracy

Despite large binaural and monaural intersubject variability, a distinct and highly significant bilateral benefit ($p < 0.0001$) was found for SLA across stimuli and test occasions (Table 1). Across annual visits, 74% - 83% (cricket chirp stimulus) and 57% - 76% (dog bark stimulus) of the subjects demonstrated BiCI SLA significantly different from chance performance ($p < 0.05$), that is EI < 0.54 (see red open circles in Figure 5 for individual cross-sectional SLA data). Thus, for the majority of the subjects, sound localization abilities existed under BiCI conditions.

Table 1. Mean speech recognition and sound localization accuracy in children with normal hearing (NH) and in children with bilateral cochlear implants (BiCI). Cross-sectional data were collected for the children with NH (Paper II), while the children with BiCI participated at three annual visits (Papers II and III).

		Children with NH (n=30)		Children with BiCI Annual visit 1				Children with BiCI Annual visit 2				Children with BiCI Annual visit 3			
		Binaural	**Monaural**	**BiCI**	**BestCI**	**Bilateral Benefit**	***n***	**BiCI**	**BestCI**	**Bilateral Benefit**	***n***	**BiCI**	**BestCI**	**Bilateral Benefit**	***n***
Speech recognition	in quiet % (SD)	98 (3)	97 (7)	87 (16)	82 (19)	5***	*57*	89 (13)	88 (12)	1	*66*	84 (14)	81 (17)	3	*63*
	in noise % (SD)	87 (7)	77 (11)	61 (20)	48 (17)	13****	*45*	66 (17)	54 (18)	12****	*52*	62 (16)	54 (16)	8****	*60*
Sound localization	cricket chirps EI (SD)	0.04 (0.07)	0.79 (0.29)	0.26 (0.28)	0.92 (0.26)	0.66****	*40*	0.33 (0.33)	0.94 (0.24)	0.61****	*66*	0.40 (0.24)	0.92 (0.30)	0.52****	*67*
	dog barks EI (SD)	0.06 (0.13)	0.73 (0.37)	0.38 (0.33)	0.96 (0.21)	0.58****	*41*	0.40 (0.33)	1.01 (0.18)	0.61****	*66*	0.53 (0.26)	0.94 (0.26)	0.41****	*67*

Under BiCI conditions, the mean (SD) EI ranged 0.26 (0.28) to 0.53 (0.26) across stimuli and test occasions (Table 1). Using a single CI (BestCI), the mean EI was close to 1, reflecting poor SLA (Table 1). Indeed, ≤10% of the subjects showed an EI < 0.54 across stimuli and visits using BestCI (see Figure 5 for individual cross-sectional data).

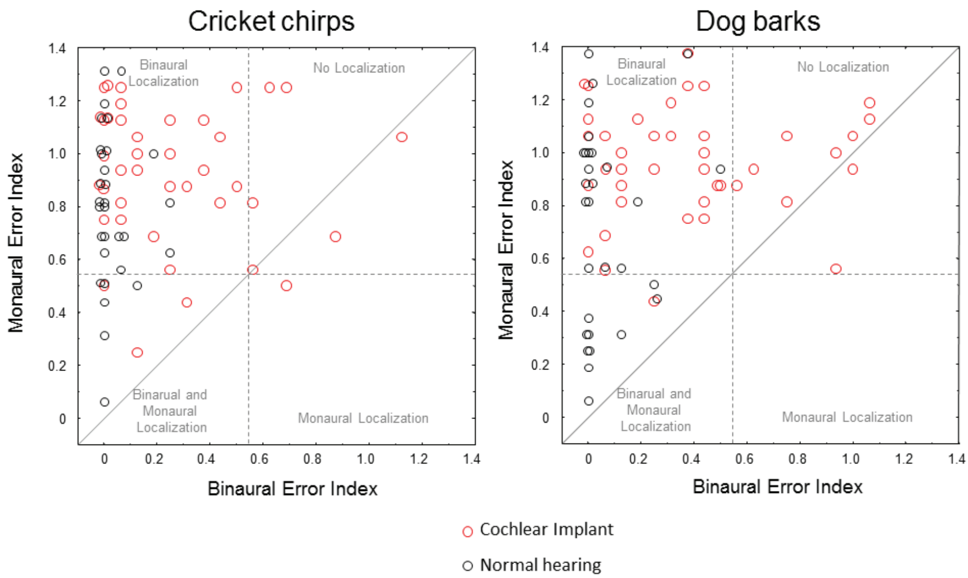


Figure 5. Individual monaural versus binaural sound localization accuracy (SLA) (cross-sectional data from the first annual visit in a longitudinal study, papers II and III). Red and black open circles represent children with bilateral cochlear implants and children with normal hearing, respectively. Markers with identical coordinates are slighlty jittered. The left and right panels illustrate SLA for a high frequency cricket chirp and a low frequency dog bark stimulus, respectively. Each panel is divided in four quadrants, to facilitate interpretation of SLA. For example, markers in the top left quadrants represent subjects showing binaural SLA, while markers in the top right quadrants represent subjects with no SLA. Markers above the diagonal lines illustrate subjects with higher binaural than monaural SLA.

4.1.1.1 The Effect of Stimulus Frequency on SLA

Cross-sectional analysis (Paper II) revealed a significant effect of stimulus frequency on BiCI SLA ($p < 0.01$), with a lower mean EI in the high frequency stimulus. No frequency-dependent difference existed in BestCI SLA ($p = 0.34$).

4.1.1.2 Perceived versus Presented Sound-Source Azimuth

To further demonstrate the higher SLA achieved using two implants, BiCI versus BestCI SLA data for the cricket chirp stimulus were illustrated in a scatterplot (Figure 6). To enable pooling of data, BestCI data are presented as if all subjects used right CI. The illustration suggest good SLA using BiCI (large circles along the diagonal), while there is a tendency of lateralization towards the active CI under BestCI conditions.

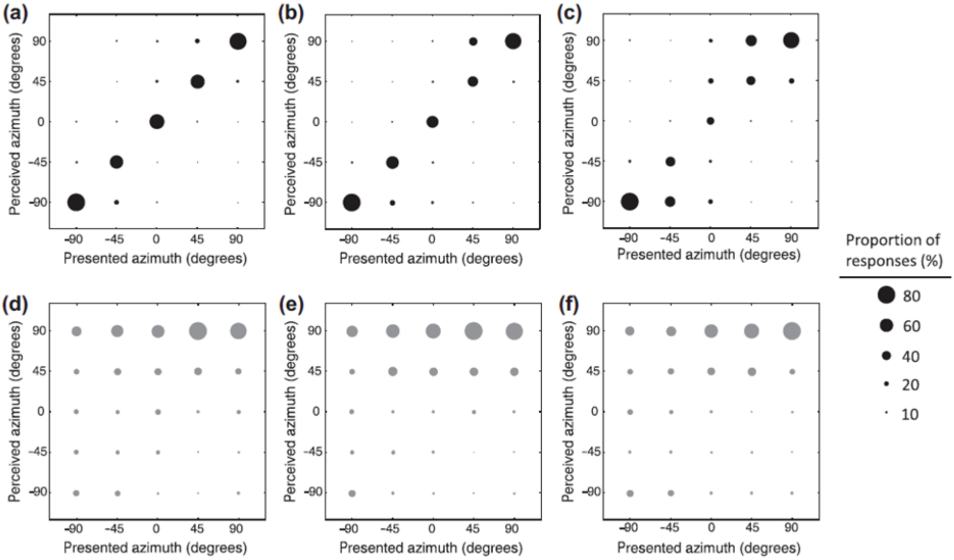


Figure 6. Scatterplot of sound localization of a cricket chirp stimulus (sound energy mainly between 2.5–5.0 kHz) under BiCI (black circles; panels a, b, and c) and BestCI (grey circles; panels d, e, and f) conditions. The size of the circles represent the proportion of correct responses for a given presented sound-source azimuth, and a scale is provided to facilitate interpretation. (a) BiCI (n = 400, 40 subjects × 10 presentations), (b) BiCI (n = 660), (c) BiCI (n = 670), (d) BestCI (n = 400), (e) BestCI (n = 660), (f) BestCI (n = 670). In the BiCI condition, sound localization accuracy is high as shown by large circles along the diagonal. For lateral azimuths -90 degrees and 90 degrees respectively, 80% and 75% of presentations were perceived correctly (data from the three visits merged). For loudspeakers at -45 degrees, 0 degrees, and 45 degrees respectively, 53%, 49%, and 49% of responses were perceived correctly. In the BestCI condition, all subjects were treated as having the CI on the right side to enable pooling of subjects using the left or right CI as their BestCI. The perceived sound was lateralized toward the side of the active cochlear implant (i.e. 45 degrees or 90 degrees azimuth) in 50%, 62%, 71%, 80%, and 77% of the presentations from loudspeakers at -90, -45, 0, 45, and 90 degrees azimuth, respectively. From Asp et al. (2015), *A longitudinal study of the bilateral benefit in children with bilateral cochlear implants*, International Journal of Audiology, 54:2, 77-88, published by Taylor & Francis.

4.1.2 Speech Recognition in Quiet and in Multi-Source Background Noise

BiCI and BestCI speech recognition in quiet was high (>80% correct across visits) and the bilateral benefit was small and clinically insignificant (Table 1). In the presence of multi-source background noise spatially separated from the target speech signal, however, the bilateral speech recognition benefit was statistically significant ($p < 0.0001$) and larger than in quiet (8%-13% across visits) (Table 1), with absolute BiCI scores ranging from 61% to 66%. Despite large intersubject variability of absolute BiCI and BestCI speech scores, a majority of the subjects achieved higher scores using BiCIs than with BestCI (72% – 83% of the subjects across visits, see Figure 7 for individual cross-sectional data from the first annual visit). A statistically significant individual bilateral speech recognition in noise benefit (more than 25.3 raus) was found in 12% – 15% of the subjects across visits.

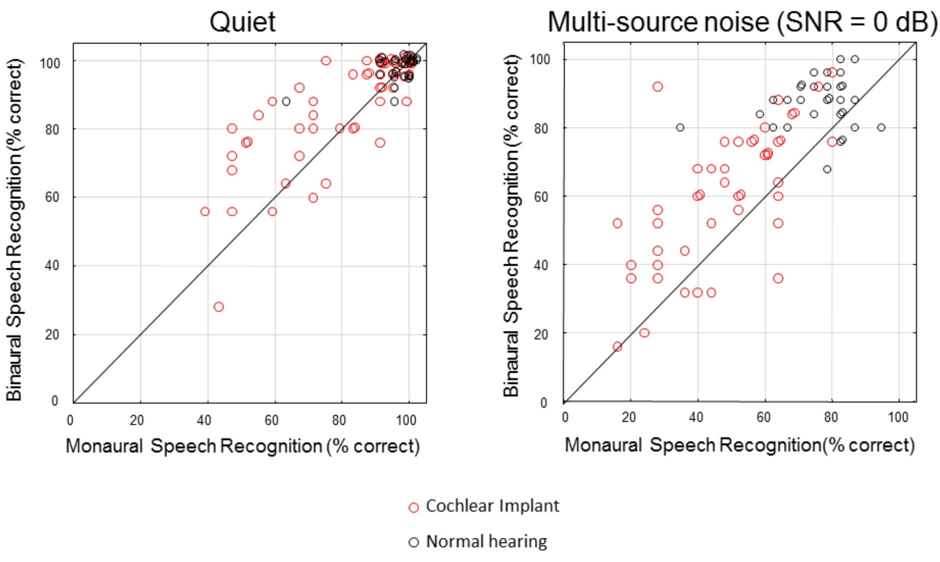


Figure 7. Individual binaural versus monaural speech recognition in quiet (left panel) and in background noise (right panel) presented from multiple spatially separate noise sources (cross-sectional data from the first visit in a longitudinal study, Paper II). Red and black open circles represent children with bilateral cochlear implants and children with normal hearing, respectively. Markers above the diagonal lines denote subjects with higher binaural than monaural speech recognition. Markers with identical coordinates are slighlty jittered.

4.1.3 Parental Reports

Paper II reports the entire result of a questionnaire distributed to parents of children with BiCI. Here, parental reports on speech recognition and sound localization abilities of their children in seven daily situations are presented (Figure 8). The daily situations were in the form of a brief statement (e.g. “My child hears everything in a noisy environment”) and parents were asked to rank their child’s ability using a single CI and BiCI. The ranking was from 1 (never) to 4 (always) and questions were formatted so that a higher rank related to better hearing performance. The median score was higher in all daily situations except the questions relating to speech understanding in quiet (Figure 8), with a significant difference between BiCI listening and unilateral CI listening in all the seven daily situations (n = 17 to 25 non-tie matched pairs available for each situation, $p < 0.001$ for all, Wilcoxon matched pairs test). Improvements after bilateral implantation in sequentially implanted children were generally observed within 6 to 12 months (89% of the parents). Overall, thus, parental reports corroborated behavioral data.

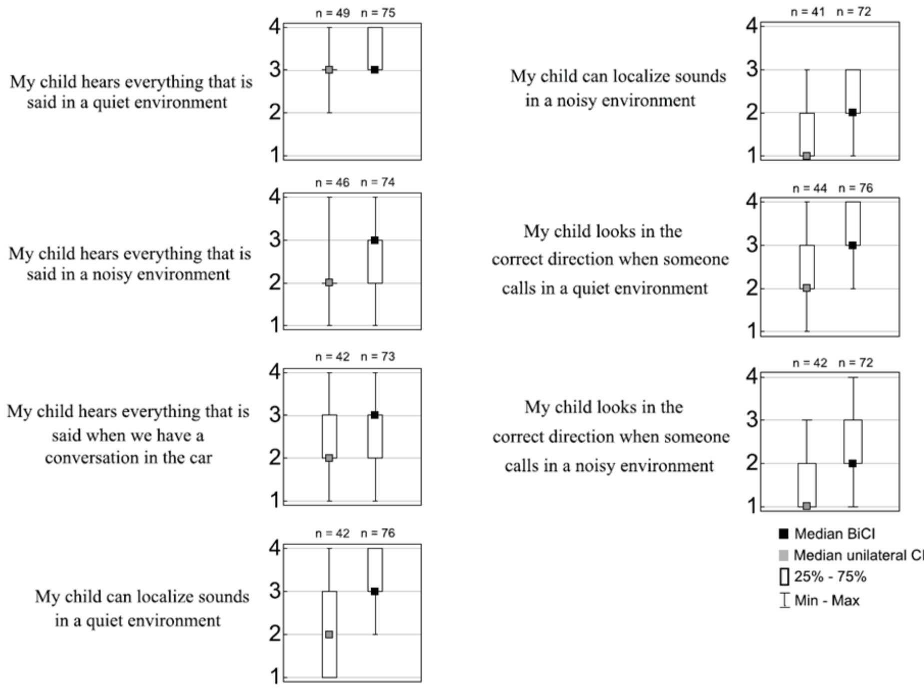


Figure 8. Boxplots of parental reports of the hearing performance of their child using BiCIs (black filled square, right side) versus a single CI (grey filled square, left side). The plots relate to parents answers in seven daily situations, which are shown to the left of each boxplot. Higher scores indicate better hearing performance. The numbers correspond to: 1 = Almost never, 2 = Approximately half of the time, 3 = Almost always, 4 = Always. A subset of parents did not have experience of unilateral implant use, or did not have experience of unilateral implant use in the specific situation; the number of parents who answered each question is indicated above the boxplots.

4.2 Spatial Hearing in Children with Normal Hearing

Speech recognition in quiet in children with normal hearing was unaffected by acute monaural conditions, with average scores of 98% and 97% for BiNH and UniNH conditions, respectively (Table 1). Individual scores are illustrated in Figure 7. In noise, however, the mean (SD) binaural speech score (87% (7)) was 10 percentage points higher than the monaural, which was similar to the bilateral benefit found in children with BiCI (8 to13 percentage points) (Table 1).

SLA in the BiNH condition was high and intersubject variability was low (mean (SD) EI = 0.04(0.07) (cricket chirps) and 0.06 (0.13) (dog barks)), while monaural plugging resulted in a large increase in EI and in intersubject variability (Table 1 and Figure 5). A majority of the normal hearing children were unable to localize the dog bark and the cricket chirp stimulus (67% and 80%, respectively) under monaural conditions (Figure 5).

4.2.1 Comparison of Performance between Children with NH and Children with BiCI

Children with NH exhibited significantly higher binaural speech recognition in quiet ($p = 0.0001$), in noise ($p < 0.0001$) and SLA ($p < 0.0001$ across stimuli) than children with BiCI (comparison based on data from the first annual visit). Table 2 summarizes the statistical comparisons (BiCI versus NH) of speech recognition data.

Under monaural conditions, children with NH showed higher SLA than children with CI (dog barks: $p = 0.001$, cricket chirps: $p = 0.04$), while the binaural EI in children with BiCI was lower than that of children with NH in the acute UniNH condition ($p < 0.0001$ across stimuli).

Table 2. Statistical analysis of speech recognition scores (converted to raus) in normal-hearing (n = 30) versus implanted (n = 57 in quiet and n = 45 in noise) children. Results from the analyses within quiet and noisy listening conditions are shown in grey areas. Results from the analyses between quiet and noisy listening conditions are shown in white areas. Significant p-values are shown in italic font. From Asp et al. (2012), *Bilateral versus unilateral cochlear implants in children: speech recognition, sound localization, and parental reports, International Journal of Audiology,* 51:11, 817-832, published by Taylor & Francis.

	BiNH (Quiet)	UniNH (Quiet)	BiNH (Noise)	UniNH (Noise)
BiCI(Quiet)	t = 4.0 *p = 0.0001*	t = 3.5 *p = 0.0007*	t = -0.90 p = 0.4	t = -3.8 *p = 0.0003*
BestCI (Quiet)	t = 5.2 *p < 0.0001*	t = 4.8 *p < 0.0001*	t = 0.69 p = 0.5	t = -2.0 p = 0.05
BiCI (Noise)	t = 12.7 *p < 0.0001*	t = 11.8 *p < 0.0001*	t = 7.2 *p < 0.0001*	t = 4.1 *p = 0.0001*
BestCI (Noise)	t = 18.6 *p < 0.0001*	t = 17.2 *p < 0.0001*	t = 11.9 *p < 0.0001*	t = 8.3 *p < 0.0001*

BiCI = Bilateral Cochlear Implants; BestCI = Unilateral CI with best speech recognition;
BiNH = Binaural condition for normal-hearing children;
UniNH = Monaural condition for normal-hearing children

4.3 The Effect of BiCI experience on SLA and Speech recognition (Papers I, II, III)

In the study sample tested with the SLA test binaurally using the pink noise stimulus, a 1:1 relationship between the median perceived and presented sound-source azimuth existed, reflecting sound localization abilities across the frontal horizontal plane (–90 to 90 degrees azimuth) (n =66, paper I). Large intersubject variability existed in chronological age (range: 2.8 – 17.3 years; median = 5.6 years), age at implantation of CI-1 (0.8 – 7.1 years; 1.9 years; n = 62 sequentially implanted subjects) and CI-2 (4.1 years; 1.6 – 14.8 years; n = 62), the interimplant interval (0.3 – 10 years; 2.1 years; n = 62), and the BiCI experience (0.1 – 3.3; mean (SD) = 1.5 (0.8)). The variability allowed analyses of the alleged effects of these subject variables. The EI (mean (SD) = 0.49 (0.34); range = 0 – 1.31) was predicted by BiCI experience, as revealed by a linear regression analysis (EI = 0.79 – 0.21 x BiCI experience (years), r = -0.51, p < 0.0001, n = 66) (Table 3).

However, no effect of chronological age, age at implantation of CI-1 or CI-2, or the interimplant interval was found, as revealed by linear regression analyses (Table 3).

Equation	r	p
EI = 0.79 – 0.21 × BiCI experience	-0.51	0.00001
EI = 0.41 + 0.032 × Age at CI-1	0.12	0.33
EI = 0.40 + 0.017 × Age at CI-2	0.15	0.22
EI = 0.48 + 0.0018 × Age	0.015	0.90
EI = 0.43 + 0.021 × Interimplant interval	0.14	0.27

BiCI = bilateral cochlear implant; CI-1 = first cochlear implant; CI-2 = second cochlear implant; EI = Error Index

Table 3. Linear regression analyses of sound localization performance (Error Index) as a function of bilateral cochlear implant experience (years), age at first and second implantation (years), age (years), and interimplant interval (years) (n = 66). From Asp et al. (2011), *Horizontal Sound Localization in Children With Bilateral Cochlear Implants: Effects of Auditory Experience and Age at Implantation*, Otology & Neurotology, 32:558-564, Published by Wolters Kluwer Health Lippincott Williams & Wilkins

Moreover, in paper II, where subjects had a longer BiCI experience, a multivariate regression analysis was applied in an attempt to model the relationship between BiCI speech recognition as well as SLA, and the same subject variables as in paper I: chronological age (range = 5.1 – 11.9; mean = 8.0 years), age at CI-1 (0.9 – 6.3 years; 2.4 years; n = 57 sequentially implanted subjects), age at CI-2 (1.6 – 9.3 years; 5.0 years; n = 57), BiCI experience (1.7 – 6.2 years; 3.3 years), and the interimplant interval (0.3 – 6.3 years; 2.6 years). For speech recognition in quiet and in noise, the forward stepwise procedure applied only included BiCI experience in the model, which in the speech in quiet condition was significant ($F(1, 55) = 4.93$, $R2 = 0.08$, $p = 0.03$) with a significant effect of BiCI experience ($b = 7.27$, $t(55) = 2.22$, $p = 0.03$). In the noise condition, however, the model was not significant ($F(1, 43) = 2.11$, $R2 = 0.05$, $p = 0.15$). For sound localization accuracy with the cricket chirp stimulus, the forward stepwise procedure only included BiCI experience in the model, which was significant ($F(1, 38) = 4.47$, $R2 = 0.11$, $p = 0.04$) with a significant effect of BiCI experience ($b = -0.10$, $t(38) = -2.11$, $p = 0.04$). For the dog barks stimulus, the forward stepwise procedure included age at CI-1 ($b = -0.07$, $t(38) = -1.34$, $p = 0.19$) and BiCI experience ($b = -0.15$, $t(38) = -2.42$, $p = 0.02$) as variables. However, the model only approached significance ($F(2, 38) = 2.96$, $R2 = 0.13$, $p = 0.06$).

4.3.1 Intrasubject Analysis of the Effect of BiCI Experience on SLA and Speech Recognition in Noise (Papers I, III)

The effect of BiCI experience on binaural SLA was also reflected intraindividually, as revealed by linear regression analyses (EI versus BiCI experience) in the 21 subjects that participated in at least 3 tests of SLA (paper I) . The time elapsed between repeated tests of SLA in a single subject ranged 0.3 – 0.8 years. The median age in this group at the initial test was the same as for the entire study group, 5.6 years (3.2 – 9.6 years, n = 21), with a mean (SD) BiCI experience at their initial test of 1.1 (0.7) years (0.1 – 2.8 years, n = 21). Individual regression lines were computed, with a resulting mean slope of -0.19 EI/year (SD = 0.29, n = 21). This reflected an improvement in EI of 19% per year, which was similar to the 21% per year found in the entire study group (n = 66).

The individual development of binaural SLA and of the bilateral speech recognition in noise benefit, was further studied in the subjects that completed all three SLA (n = 34) and all three speech in noise (n = 37) assessments between on average 3.3 years (range: 2.0 – 6.2 years) and 5.3 years (range: 3.9 – 8.2 years) of BiCI experience (paper II). The complete data set (BiCI versus BestCI) achieved in this subgroup allowed a longitudinal analysis of the effect of a relatively prolonged period of bilateral cochlear implant use. Group data for BiCI and BestCI SLA and speech recognition in noise are shown in Figures 9 and 10, respectively.

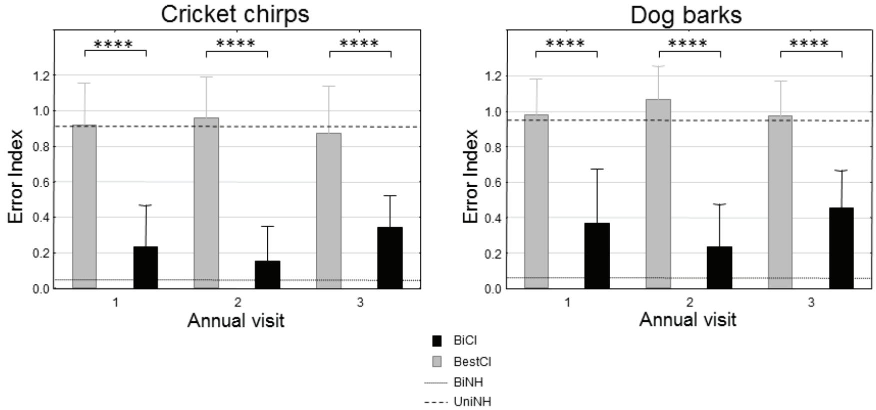


Figure 9. Mean sound localization accuracy (SLA) under BiCI (black) and BestCI (grey) listening conditions, as a function of annual assessment. Error bars denote 1 standard deviation. Dotted and dashed lines illustrate mean binaural (bottom line) and acute monaural (top line) performance, respectively, in the children with normal hearing (n = 30). A statistically significant bilateral sound localization benefit is indicated by asterisks (****p < 0.0001). From Asp et al. (2015), *A longitudinal study of the bilateral benefit in children with bilateral cochlear implants,* International Journal of Audiology, 54:2, 77-88, published by Taylor & Francis.

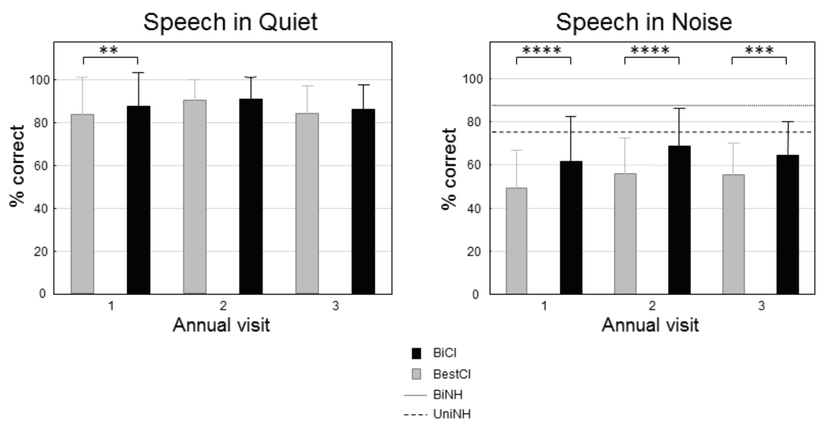


Figure 10. Mean speech recognition in quiet (left) and in spatially separate multi-source noise (right) as a function of visit (n = 48 in quiet, n = 37 in noise). Bilateral (BiCI, black bars) and best unilateral conditions (BestCI, grey bars) are shown for subjects using cochlear implants. Whiskers denote 1 SD. Dotted and dashed horizontal lines illustrate average binaural (upper line) and monaural (lower line) speech recognition in noise, respectively, for the normal-hearing children (n = 30). A statistically significant bilateral speech recognition benefit is indicated by asterisks (**p < 0.01, ***p < 0.001, ****p < 0.0001). From Asp et al. (2015), *A longitudinal study of the bilateral benefit in children with bilateral cochlear implants*, International Journal of Audiology, 54:2, 77-88, published by Taylor & Francis.

Intrasubject linear regression analyses of the SLA data revealed a mean (SD) slope of 0.06 (0.12) EI/year ($p = 0.01$, $Z = 2.57$) for the high frequency cricket chirp stimulus, which corresponded to a decrease in SLA of 6% per year. The parallel analysis for the low frequency dog bark SLA data did not reveal a mean slope that was significantly different from zero ($p = 0.18$, $Z = 1.34$). This small deterioration in localization accuracy of the high frequency stimulus implied supplementary detailed analysis of individual data since it was unexpected given previous findings [28, 40, 57, 66-69]. Inspection of developmental patterns indicated that BiCI SLA was consistently significantly better than chance performance (EI < 0.54) in most of the children (74%, cricket chirp stimulus; 50%, dog bark stimulus), while the remaining children showed either a pattern of developing SLA (9%, 9%), or a pattern of fluctuating SLA (18%, 41%). In an attempt to understand the reasons for the variable pattern of the substantially smaller “fluctuating group” versus the “stable group”, post-hoc analysis of the subject variables age at implantation, the interimplant interval, and the BiCI experience was applied. Subjects in the “stable group” were on average implanted with the first and second cochlear implant earlier and had a shorter interimplant interval than subjects in the “fluctuating group” (cricket chirps: CI-1: $p = 0.0003$, CI-2: $p = 0.0003$, interimplant interval: $p = 0.03$; dog barks: CI-1: $p = 0.02$, CI-2: $p = 0.002$, interimplant interval: $p = 0.009$), suggesting the timing of implantation to have an effect on consistent SLA.

Large intrasubject variability in the bilateral speech recognition in noise benefit existed (cf. Figure 4 in Paper III) and development of absolute and relative data was studied using linear regression analyses. Neither binaural nor monaural development in performance was found, as revealed by comparing the mean of the individual slopes obtained using linear regression analyses (mean (SD) slope binaural: 1.1 (11.0) raus/year; mean (SD) slope monaural: 2.6 (9.6) raus/year, $n = 37$) to zero ($p > 0.05$). The bilateral benefit was also stable over time, demonstrated both in the group data (Bilateral benefit = 7.5 + 0.9 × BiCI experience, $r = 0.08$, $p = 0.39$, $n = 111$ (3 visits × 37 subjects) and within subjects (mean (SD) slope = -1.5 (9.2) raus/year, $n = 37$) ($p = 0.33$).

4.4 The effect of early bilateral implantation on SLA

An effect of age at CI-2 – the age at which bilateral electrical stimulation started – was found on the bilateral SLA benefit, both for the high frequency ($r = 0.39$, $p = 0.0006$, $n = 75$) and for the low frequency ($r = 0.42$, $p = 0.0002$, $n = 74$) stimulus (1 to 3 measurements averaged per subject, paper III).

Furthermore, children implanted bilaterally by 4 years of age demonstrated an improvement in EI with increasing BiCI experience which was almost twice as fast as in children implanted after 4 years of age (CI-2 $\leq$ 4 years: EI = 0.98 – 0.31 × (BiCI experience), $r = -0.57$, $p < 0.001$, $n = 34$: CI-2 > 4 years: EI = 0.72 – 0.16 × (BiCI experience), $r = -0.43$, $p < 0.05$, $n = 32$) (paper I). This effect was also reflected intraindividually ($n = 21$), as indicated by comparing the mean (SD) of the slopes of the individual regression in children bilaterally implanted by age 4 years (–0.23 (0.21) EI/year, $p < 0.01$, $n = 10$) and after 4 years of age (– 0.17 (0.35) EI/year, $p = 0.15$, $n = 11$) (p-values reflect statistical comparison to zero slope).

4.5 Sound Localization Accuracy in Infants and Adults with Normal Hearing as Measured with a Corneal Reflection Eye Tracking Technique

Employing a newly developed method, which allowed pupil positions to be objectively and precisely recorded using a corneal reflection (CR) eye tracking technique, horizontal SLA was rapidly measured in children (mean = 168 seconds, $n = 12$) and adults (mean = 162 seconds, $n = 8$) with NH. Subject characteristics and descriptive statistics from the tests in infants are summarized in Table 4.

Table 4. Subject characteristics (children, n = 12) and descriptive statistics from the test of horizontal sound localization accuracy (SLA): Error Index (EI), age, time elapsed for a test of SLA, the number of sound-source shifts that a subject participated to before the test was terminated, the number of perceived sound-sources that was possible to quantify based on the analysis paradigm described in the method, and the auditory-visual EI. Subjects are sorted in ascending EI order.

	EI	Age (weeks)	Time elapsed for a test of SLA (seconds)	Number of sound-source shifts	Number of perceived sound-sources	Auditory-visual EI
	0.15	104	134	24	24	0
	0.24	66	168	24	13	0.093
	0.25	102	170	24	19	0.035
	0.30	157	103	10	8	0.24
	0.35	52	263	24	18	0.019
	0.40	74	199	24	21	0.15
	0.41	42	117	13	9	0.18
	0.45	36	184	19	15	0.24
	0.52	57	251	23	15	0.33
	0.56	29	129	15	12	0.29
	0.63	42	141	15	12	0.024
	0.74	31	159	17	12	0.056
Mean	0.41	66	168	19	14	0.14
SD	0.17	38	50	5	5	0.11

Thorough visual inspection of gaze data in children indicated that gaze shifts occurred in sound-only periods. The medians of the perceived sound-source azimuths either coincided with the presenting sound-source azimuth, or were offset by a maximum of 20 degrees in children (left panel in Figure 11). In contrast, adults revealed a perfect match from -55 to 55 degrees, except at 15 degrees azimuth (median=20 degrees) (left panel in Figure 11).

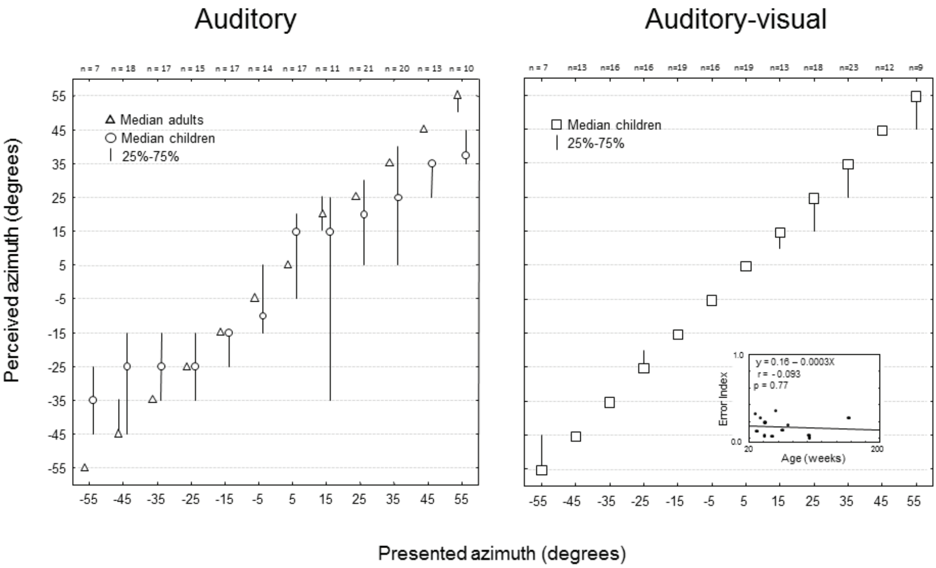


Figure 11. Median perceived azimuths versus presented azimuths using auditory (left panel) and auditory-visual (right panel) stimuli. Children are denoted by open circles (auditory) and open squares (auditory-visual) and adults are depicted by open triangles (auditory). Error bars denote quartiles (25% - 75%) (children: n = 179 perceived auditory azimuths, n = 181 auditory-visual azimuths; adults: n = 190 perceived auditory azimuths). The numbers in the top of the Figure correspond to the number of perceived azimuths per presented azimuth in children. For auditory presentation, the median perceived azimuth coincided with the presented azimuth in adults (except for 15 degrees azimuth), whereas an offset of 0 to 20 degrees existed in children. The quartile ranges of the perceived auditory azimuths were larger in children than in adults, indicating higher intersubject variability in children. Specifically, the majority of quartile ranges in adults were zero (except for -45, 15, and 55 degrees), demonstrating high horizontal sound localization accuracy and low intersubject variability across the entire spatial range tested. For auditory-visual presentation, the median perceived azimuths coincided with the presented azimuths in children, with 6/12 quartile ranges = 0 degrees and the remaining 6/12 quartile ranges within 10 degrees. A similar 1:1 relationship between median perceived and presented azimuths was demonstrated in adults (not shown). Inset: No relationship was found between the auditory-visual Error Index and age in children, suggesting a mature oculomotor function in the frontal horizontal plane in the tested age range. The left panel of the Figure is From Asp et al. (2015), *Corneal-Reflection Eye-Tracking Technique for the Assessment of Horizontal Sound Localization Accuracy From 6 Months of Age,* Ear & Hearing, published ahead of print by Wolters Kluwer Health Lippincott Williams & Wilkins.

Children showed a mean (SD) EI of 0.42 (0.17), which was significantly higher than in adults (mean (SD) = 0.054 (0.021)) ($p < 0.0001$). However, children revealed a distinct age-related EI improvement of 16 percentage points per year (EI = 0.619 – 0.003 × Age (weeks), $r = -0.68$, $p = 0.015$, $n = 12$), suggesting an ongoing maturation of SLA in the studied age range (29 – 157 weeks) (Figure 12).

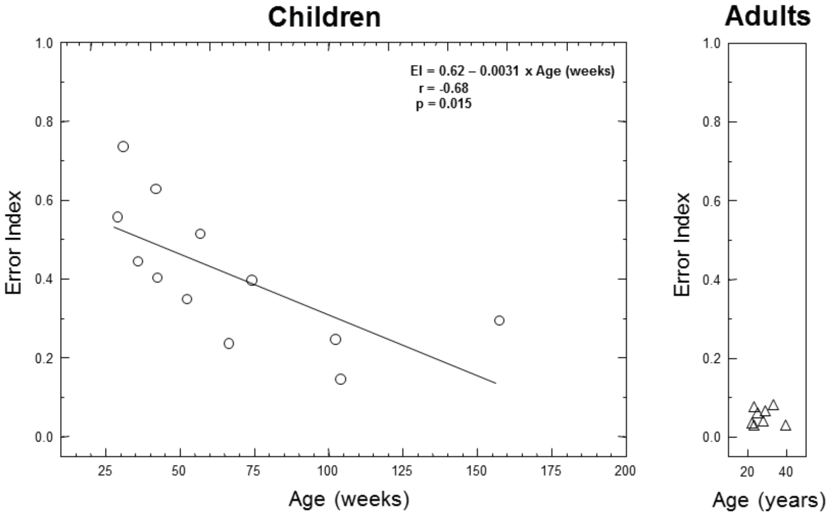


Figure 12. Horizontal sound localization accuracy, quantified by an Error Index, as a function of age in children (left panel, open circles) and adults (right panel, open triangles). In children, linear regression analysis (EI versus Age (weeks)) showed a decreasing Error Index with increasing age (n = 12), that is, an age-related improvement of sound localization accuracy (SLA). High SLA was found in all the adults (n = 8). From Asp et al. (2015), *Corneal-Reflection Eye-Tracking Technique for the Assessment of Horizontal Sound Localization Accuracy From 6 Months of Age,* Ear & Hearing, published ahead of print by Wolters Kluwer Health Lippincott Williams & Wilkins.

4.5.1 Auditory-Visual Localization Accuracy as a Measure of Oculomotor Maturity

To study if oculomotor immaturity could be a confounder for the effect of age on SLA, we computed the auditory-visual EI in adults (mean (SD) = 0.016 (0.022); range = 0 – 0.050) and children (mean (SD) = 0.139 (0.114); range = 0 – 0.327). In children, no effect of age on the ability to follow the auditory-visual stimulus existed, as revealed by simple linear regression analysis (auditory-visual EI = 0.158 – 0.0003 x Age (weeks), $r = -0.093$, $p = 0.77$, $n = 12$) (inset in right panel in Figure 11) and by analysis of the perceived auditory-visual azimuths as a function of presented auditory-visual azimuths which demonstrated a 1:1 relationship between the median perceived auditory-visual azimuths and presented auditory-visual azimuths (right panel in Figure 11).

4.5.2 Reliability

The eight adults showed high reliability as demonstrated by the low variability in test–retest differences (mean (SD) = 0.013 (0.039); 95% C.I. = [-0.020; 0.046]) (right panel in Figure 13). The 95% C.I. for a single SLA measurement in adults was estimated to ±0.054 (see equation 2 in Subjects and Methods). The "test – retest" differences in children were symmetrically distributed around zero, with a mean (SD) of 0.015 (0.161) (left panel in Figure 13). The 95% C.I. of the "test – retest" differences [-0.087; 0.117] included zero, that is, no significant learning effect existed. Crucially, the 95% confidence interval for the EI for a single SLA measurement in children was estimated to ±0.12 (see equation 1 in Subjects and Methods).

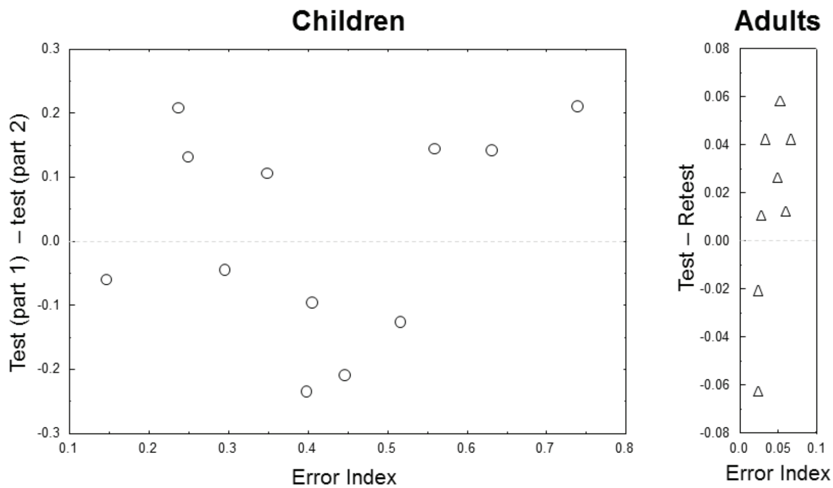


Figure 13. Test (part1) – test (part2) as a function of Error Index in children (left panel, open circles) and test – retest as function of Error Index in adults (right panel, open triangles). The "test – retest" for children was calculated by dividing each test in two parts and subtracting the Error Index of the final part of the test from the Error Index of the first part of the test, while sound localization accuracy was assessed twice in adults (i.e. test and retest). The horizontal dashed line indicates no difference between test and retest. Test – retest differences in adults were close to zero. In children, "test – retest" differences were symmetrically distributed around zero and larger than in adults, albeit, no significant difference between the mean Test – Retest difference in children and adults existed (p = 0.91, Mann-Whitney U test). From Asp et al. (2015), *Corneal-Reflection Eye-Tracking Technique for the Assessment of Horizontal Sound Localization Accuracy From 6 Months of Age*, Ear & Hearing, published ahead of print by Wolters Kluwer Health Lippincott Williams & Wilkins.

5. Discussion

5.1 Bilateral versus Unilateral Cochlear Implants

As a major part of this thesis, children with BiCI were assessed using two versus one CI for speech recognition in quiet, in noise presented from multiple spatially separate noise interferers, and sound localization accuracy in the frontal horizontal plane (papers II and III). The within-subject evaluations revealed a significant bilateral speech in noise benefit (ranging on average from 8 to 13 percentage points), while speech recognition in quiet was comparable between binaural and monaural conditions. A large and highly significant bilateral SLA benefit was demonstrated, using both high- and low frequency auditory stimuli. In no measures was the bilateral benefit uniform across subjects. On average, however, it continued to exist over time, at least until 5 years of bilateral cochlear implant use.

Overall, these findings are in good agreement with those previously reported, both for within- and between subject comparisons [15, 38-43]. However, no randomized trials aiming to study the alleged benefits afforded by BiCI over a single CI are currently available. A recent review synthesizing best-evidence indicates that while BiCI may be useful in sound localization, there is weak support for any effect on speech recognition [44]. Indeed, in papers II and III, a minority of the subjects showed an individual bilateral speech recognition benefit that was statistically significant. Further, the speech recognition in noise benefit seems to be dependent on the incidence of the noise (e.g. towards CI-1 or CI-2), and on the existence of a spatial separation between noise and target signal [15, 43, 70-72].

Spatial hearing performance in children with BiCI after a relatively prolonged period of BiCI use is not well documented. In this thesis, longitudinal relative data on the perceptual benefits provided by BiCI between on average 3.3 years to 5.3 years after bilateral cochlear implantation is reported (paper III). Since experience plays a critical role for normal development and maintenance of auditory structures [73], a comparison of our findings with previous studies may be confounded by children's relative auditory experience with BiCIs (see subheading 5.2 below). Therefore, two studies including subjects with at least 3 years of BiCI experience and reporting relative speech recognition data were identified [74, 75]. Those studies reported a bilateral speech recognition in noise benefit of 10 to 16 percentage points, which is similar in magnitude to that presented here, while the bilateral speech in quiet benefit was larger than in this thesis.

The proportion of subjects that localized broadband sounds better than random performance (paper I, 62%) was similar to those previously reported (48% and 63%) [67, 76]. The proportion was slightly higher for the high pass sound (papers II and III, 74% - 83% across visits), which may be explained by the relative experience with BICI, although it is also likely that the increased difficulties in the setups used in those other studies may have contributed (e.g. increased spatial resolution). Moreover, a significant effect of stimulus frequency on BiCI SLA existed, with higher accuracy in the high-frequency stimulus (paper II). This is consistent with the idea that individuals with BiCI primarily are sensitive to ILD cues [77]. Nonetheless, the majority of the subjects in papers II and III localized the low-frequency stimulus (with the main spectral energy < 1 kHz) significantly better than random performance using BiCIs, suggesting the use of ITD cues for localization. However, even if the high frequency information for the low frequency stimulus was some 30 dB below the low-frequency part of the stimulus (see Figure 2 in paper II) there still is a possibility that it was audible through the CIs, thus providing ILD cues. Indeed, access to ITDs is reported to be minimal in both adults [e.g. 78, 79] and children [80] using BiCIs.

5.2 Experience-driven Maturation of Sound Localization

We found an improving sound localization accuracy with increasing BiCI experience (about 20 percentage points/year) the first 3 years of BiCI use, both on group level and individually (paper I). Subsequently, SLA seemed to plateau between approximately 3 to 5 years of BiCI experience on average (paper III). No effect of age at test was found.

The development of SLA after onset of bilateral stimulation – previously documented in smaller samples of children with BiCI [40, 67] – may be explained by an experience-dependent plasticity of the structures in the central auditory system underlying spatial hearing. Support for the dependence of experience for developing spatial hearing can be found in both animal and human studies. In the barn owl, calibration of auditory space is performed with the help of visual cues and the owl can adapt to altered visual feedback [81], while adult ferrets can relearn to localize with altered spatial auditory cues (monaural plugging) with eyelids sutured [82]. In those ferrets, a reweighting of spatial cues was observed, with sensitivity shifted away from the cues that were most affected by the monaural plug. In humans, as elegantly shown by modifying pinnae (and hence the head-related transfer functions) with molds, the system for localization of sound is shaped in a learning process, similar to what appears to occur in animals [83]. Indeed, multiple central representations of auditory space seem to develop in both ferrets and humans, demonstrated by the ability to localize both with and without altered spatial cues after training. In all, experience seems crucial for the development of sound localization.

The effect of experience may be particularly strong during certain periods during development [84]. It is shown in Mongolian gerbils, for example, that sensitivity to ITD undergoes a developmental maturation after hearing onset and that this development is disrupted when the gerbils are reared in white noise [51]. As another example, the neural representation of ITD is degraded when deafness is congenital as compared to acute in cats [85]. Also, during postnatal development in rats, binaural integration of ILD is disrupted by introducing monaural deprivation [50]. Hence, important sound localization cues are shaped by the inexperience of distinct binaural cues during sensitive periods in these animals.

Human studies further suggest stimulus-driven auditory plasticity at the level of the brainstem, as demonstrated by ongoing maturation of the brainstem response to speech sounds and clicks up to 4 years of age [53, 86], and altered subcortical responses after pitch-discrimination training in adults [87].

Children who receive BiCI in sequential procedures – as the majority in this thesis did – will undeniably have to relearn localization in the transition from unilateral to bilateral CI. Animal evidence suggests that efferent auditory pathways have a role in this plasticity and that the olivocochlear (OC) system – a component of the auditory efferent system projecting from the superior olivary complex to the cochlea – is needed for relearning localization (during unilateral HL in ferrets) [88]. Although the OC system is not necessarily involved in the plasticity of spatial hearing in humans, the existence of neural feedback somewhere in the central auditory system seems likely: as pointed out by Irving [88], if no efferent control based on prior auditory experience would exist, the high accuracy with which adult humans can pinpoint sound-sources along the horizontal dimension would have to rely on identical interaural hearing sensitivity, which is rarely found [89].

5.3 The Effect of Early Bilateral Implantation On Spatial Hearing

Age at bilateral implantation – the age at which binaural cues may at all be transmitted to children with bilateral profound hearing loss – did not show an effect on either BiCI SLA, BestCI SLA, or speech recognition scores (papers I and III). In addition, children with relatively late access to bilateral hearing (> 4 years of age) demonstrated a bilateral benefit (paper III). However, linear regression analyses indicated that the bilateral SLA benefit was greater in children with early bilateral implantation (paper III). That is, the discrepancy between monaural and binaural localization abilities was more pronounced in children with early access to binaural cues. In addition, the rate of development in SLA as a function of BiCI experience from 0 to 3 years post bilateral implantation was almost twice as fast in subjects implanted bilaterally by 4 years of age as compared to children implanted after 4 years of age, which was confirmed both in the entire study group and individually (paper I). Furthermore, analysis of individual developmental patterns in SLA revealed that children with late bilateral implantations and relatively long interimplant intervals showed an ability to localize at one visit, followed by unexpected poor localization accuracy at a follow-up one year later, possibly owing to inconsistent use of BiCI (paper III).

A possible explanation for the effects of the timing of bilateral implantation, is that some of the subjects with late bilateral implantation experienced a prolonged period of unilateral stimulation, a factor contributing to disruption of bilateral auditory pathways and reorganization of auditory cortex in children born deaf [90]. The importance of early access to binaural cues for SLA has previously been demonstrated in children with hearing impairment [91], and several animal studies [e.g. 50, 51, 92].

Importantly, however, late bilateral implantation may still offer perceptual benefits, as shown by increased speech recognition in adolescents receiving sequential bilateral implantation as late as at a mean age of 13.5 years [93]. Also, a self-perceived bilateral benefit seem to exist as demonstrated by the consistent use of BiCI reported by the parents of the participating children in paper II and elsewhere [94].

Notwithstanding the documented positive effects of BiCI found in children with relatively late bilateral implantation, early provision of BiCI should be the standard treatment for children with bilateral severe-to-profound hearing loss and also, perhaps, for children with severe unilateral hearing loss on the basis of the "aural preference syndrome". Unilateral hearing loss – as in children with a single CI – results in an abnormal aural preference for the ear with better hearing with cortical reorganization [reviewed in 95] and reduced binaural sensitivity [96] as possible consequences. Some potential of reversing the reorganization is however suggested, as found by recording local field potentials from the cortical surface of congenitally deaf cats with unilateral cochlear implants fitted at various developmental points [97].

5.4 Comparison of Performance between Children with NH and Children with BiCI

Consistent with earlier findings [e.g. 15, 41], BiCI speech recognition in noise and SLA was not restored to performance levels obtained in children with NH (aged 5 to 9 years) (paper II), even after several years of BiCI experience (mean = 5.3 years at the final assessment in paper III). Limited spectral resolution in the implant and audio processor hardware, temporal mismatch due to unsynchronized left and right CIs, and mismatched place of stimulation due to different insertion depths of the implant electrodes in the cochleae, are possible reasons for distortion of binaural cues and worse outcomes in children with CI [34, 49, 98-100]. Furthermore, as found in papers I and II, the auditory experience after BiCI, as well as the severity and extent of the hearing loss experienced prior to implantation, contribute to performance [28, 48, 57, 66, 101, 102]. Some of the above mentioned factors should be possible to influence. For example, paradigms for binaural fitting of BiCIs should be explored, maximizing the fusion of left and right signals through careful pitch-matching of interaural electrode pairs. Preferably, such paradigms should not require behavioral responses (i.e. when fitting BiCI to infants). Instead, electrophysiological recordings of auditory brainstem responses, such as the binaural interaction component [103], or interaural comparisons of wave latencies, could be explored. As another example, synchronization of left and right CI could improve the usually poor ITD sensitivity in subjects with CI, who generally show ITD thresholds that are 10 times that of individuals with NH on average [48].

5.5 Sound Localization in Infants and Adults with Normal Hearing

By objectively recording gaze towards spatially distributed auditory and visual stimuli using a CR eye tracking technique, we assessed SLA in infants and children (6 to 36 months) who passed the neonatal newborn hearing screening and in otologically normal adults. The automatic acquisition of gaze behavior, minimal need for instructions, continuous broad-band auditory stimulus with visual reinforcement, and random assignment of presenting sound-source azimuth, allowed for assessment of SLA in less than 3 minutes on average. High SLA across the entire spatial range (± 55 degrees azimuth), high test – retest reliability, and low intersubject variability existed in adults. Infants showed significantly higher EI (lower SLA) than adults, with an age-related improvement in SLA of about 16 percentage points per year. This improvement was unrelated to relative maturity of oculomotor function, as revealed by linear regression analysis (auditory-visual EI as a function of age) and as demonstrated by the 1:1 relationship between perceived and presented auditory-visual azimuths. Furthermore, estimation of test variance for an individual child showed relatively high reliability in EI (95% C.I. = [-0.12; 0.12]).

Few studies have evaluated horizontal SLA in very young children. Rather, spatial resolution (i.e. the discrimination threshold for the angular difference between two sound-sources) has been the focus of study [e.g. 104, 105, 106], perhaps because of the convenient nature of observer-based assessment of responses such as left versus right head-turns in prelingual subjects. This localization acuity, however, seems to involve different cortical processes than those utilized for absolute localization accuracy [107]. Furthermore, head-turn angels are not necessarily related to the visual axis (gaze) [108]. To measure the perception of the actual source of a sound, thus, require accurate behavioral responses from the listener. The feasibility of using gaze as a measure of the perceived sound-source is not unexpected. Looking towards sound-sources is a natural behavior that is “practiced” daily. Certainly, auditory targets can be used to evoke saccadic eye movements in humans [109] and stable fixations and adult-like amplitude of saccades are exhibited already from a few weeks of age [110]. In fact, just minutes after birth, neonates orient their eyes toward sound [111].

Several findings in paper IV demonstrate that the use of gaze as a measure of the perceived locus of a sound rapidly provided valid and objective data on sound localization accuracy in infants. First, across the entire spatial range (±55 degrees), the median perceived sound-source azimuths either coincided with, or were within 20 degrees from, the presented sound-source azimuths. Second, thorough visual analysis of the patterns of pupil positions in all the participating children indicated that they adjusted their gaze in response to the continuously updating sound-source positions (see Supplemental Digital Online Content in paper IV which provides examples of three children demonstrating extreme and median EI). Third, the systematic improvement of SLA as a function of age is well in line with previous head-turn data on the development of infant absolute sound-source identification between 6 and 18 months of age [58].

The data from the test of SLA in adults were highly reliable, as shown by test–retest differences close to zero and low test–retest variability (mean = 0.013, 95% C.I. = [-0.020; 0.046]). The range of EI (0.031 to 0.084) was well in line with previous studies in NH subjects using the EI as an outcome measure and broadband or low frequency stimuli (EI-range: 0.023 to 0.10) [28, 59, 61, 112]. Despite the short time needed for data acquisition (mean = 162 seconds, n = 8), we could not identify any adult sound localization studies in NH listeners that reported higher SLA than reported in paper IV [25, 113-117]. Possible reasons for the higher SLA found in paper IV include the lack of roving of the stimulus level (although spectral variation between loudspeakers was low and the intensity of the stimulus itself varied over time and across spatial shifts), and the possibility for listeners to sample the ongoing auditory stimulus by head-movements [25, 118]. However, gaze – as measured by CR eye tracking – may be a more accurate measure of SLA than, for example, head-pointing or verbal indication of the perceived sound-source azimuth [25, 113, 116, 117]. Under highly dynamic conditions, for example, such as when the head is moving during sound presentation, gaze seems to come closer to auditory targets than the head angle, which tends to undershoot the target [119]. In addition, participants of a head-pointing task also use movements of the eyes to localize the target [25, 113].

5.6 Future Directions – Sound Localization as a Tool for Clinical Purposes and Research

Poor spatial hearing poses a large auditory handicap according to subjective reports [120]. However, standard clinical hearing tests, such as measuring sensitivity to sound in quiet, is not sufficient to assess functional deficits in spatial hearing. The objective and rapid method for assessing SLA proposed in this thesis make available a tool for the study of SLA throughout the life span. Given the great clinical need for behavioral measures in pre-verbal subjects, the reliable assessment of SLA obtainable using CR eye tracking should provide a valuable tool for clinicians and clinical researchers alike. Assessment of SLA in individuals with experimentally manipulated spatial cues (either anatomically or through design of various stimuli) and in individuals with various forms of hearing loss, varying prior auditory experience, and of different ages, may aid in the understanding of some fundamental aspects related to plasticity in spatial hearing. In addition, with the provision of cochlear implants and/or hearing aids at an ever younger age in children, a routine follow-up of spatial hearing starting as early as possible should benefit the child and assist in the binaural/bimodal fitting process already during infancy. There may also be a value in assessing SLA in individuals with unilateral or mild hearing loss, since they perceive a significant auditory handicap, noticeably with negative effects on quality of life in children [121, 122].

6. CONCLUSIONS

Speech recognition in noise presented from multiple spatially separate interferers, and sound localization accuracy of high and low frequency sounds in the frontal horizontal plane is better with bilateral cochlear implants than with a unilateral cochlear implant in bilaterally implanted children. Speech recognition in quiet is comparable under bilateral and unilateral listening conditions. Parental reports confirm these behavioral findings. While the bilateral speech in noise and SLA benefit is not uniform across children with BiCI, it continues to exist, on average, until at least 5 years after bilateral implantation.

During the first 3 years after bilateral cochlear implantation, BiCI SLA emerges as a function of experience with BiCI, possibly owing to the ongoing stimulus-driven maturation of the central auditory system. Between about 3 and 5 years after bilateral implantation, SLA plateaus in subjects who received BiCI relatively early in life. Moreover, early bilateral implantation seems to promote a faster development of SLA as a function of BiCI experience, and a larger bilateral benefit may be achieved when BiCIs are provided early. However, spatial hearing in children with BiCI remains poorer than in children with NH. Overall, assessment of absolute horizontal SLA and speech recognition in multi-source noise reveal spatial hearing deficits in children with BiCI as compared to children with NH.

Corneal reflection eye tracking provides an objective and fast assessment of horizontal SLA from about 6 months of age, and may enable gaze to be used as an objective measure for sound localization throughout the life span. Infants with NH reveal immature SLA, with systematic improvements related to increasing age. Adults with NH show high overall SLA, and low intra- and intersubject variability in sound localization accuracy.

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